# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

| | | |
|---|---|---|
| Applicant's or agent's file reference<br>03678207PC00 | **FOR FURTHER ACTION** | See item 4 below |
| International application No.<br>PCT/US2004/035396 | International filing date *(day/month/year)*<br>21 October 2004 (21.10.2004) | Priority date *(day/month/year)*<br>21 October 2003 (21.10.2003) |
| International Patent Classification (8th edition unless older edition indicated)<br>See relevant information in Form PCT/ISA/237 | | |
| Applicant<br>INSPIRE PHARMACEUTICALS, INC. | | |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

| | | |
|---|---|---|
| ☒ | Box No. I | Basis of the report |
| ☐ | Box No. II | Priority |
| ☒ | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☐ | Box No. IV | Lack of unity of invention |
| ☒ | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| ☐ | Box No. VI | Certain documents cited |
| ☐ | Box No. VII | Certain defects in the international application |
| ☐ | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

| | |
|---|---|
| | Date of issuance of this report<br>24 April 2006 (24.04.2006) |
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br>Facsimile No. +41 22 740 14 35 | Authorized officer<br>Philippe Becamel<br>Telephone No. +41 22 338 70 90 |

Form PCT/IB/373 (January 2004)

# PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

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## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

| | |
|---|---|
| Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) | |
| Applicant's or agent's file reference<br>see form PCT/ISA/220 | **FOR FURTHER ACTION**<br>See paragraph 2 below |
| International application No.<br>PCT/US2004/035396 | International filing date *(day/month/year)*<br>21.10.2004 |
| Priority date *(day/month/year)*<br>21.10.2003 | |
| International Patent Classification (IPC) or both national classification and IPC<br>A61K31/52, A61P29/02 | |
| Applicant<br>INSPIRE PHARMACEUTICALS, INC. | |

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Loher, F

Telephone No. +49 89 2399-7839

# WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/035396

## Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-16 (IA)

because:

☒ the said international application, or the said claims Nos. 1-16 (IA) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

**see separate sheet**

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | 2-11,15,16 |
| | No: | Claims | 1,12,13,14 |
| Inventive step (IS) | Yes: | Claims | 2-11 |
| | No: | Claims | 1,12-16 |
| Industrial applicability (IA) | Yes: | Claims | - |
| | No: | Claims | |

2. Citations and explanations

**see separate sheet**

Re Item III

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 1-16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

D1: EP-A-0 066 918 (THE PROCTER & GAMBLE COMPANY) 15 December 1982 (1982-12-15)
D2: EP-A-1 348 466 (INSPIRE PHARMACEUTICALS, INC) 1 October 2003 (2003-10-01)

If not mentioned otherwise, the relevant passages are those mentioned in the International Search Report.

**Art 33(2)** The present application does not meet the requirements of Article 33(2) PCT, since the subject-matter of claims 1, 12, 13 and 14 is not new.

D1 discloses an analgesic composition comprising adenosine derivatives (especially compound X) falling within the scope of present formula (I). The oral, intravenous and topical use is disclosed as well. Therefore, the subject-matter of claims 1, 12, 13 and 14 is not new in the light of D1.

**Art 33(3)** The present application does not meet the requirements of Article 33(3) PCT, since the subject-matter of claims 1, 12, 13 and 14 does not seem to involve an inventive step.
D2, which is considered to represent the most relevant state of the art, discloses the use of purine P2X receptor antagonists in the treatment of pain, in particular traumatic pain, neuropathic pain, inflammatory pain, acute pain, chronic pain, organ or tissue pain, and pain associated with diseases.
The problem to be solved by the present invention may therefore be regarded as how to provide an improved medicament for the treatment of pain.
The present application suggests to solve the problem posed by providing P2X receptor antagonists as defined by present formula (I).

D1 discloses an analgesic composition comprising a compound falling within the scope of present formula (I).

Taking into account the teaching of the cited prior art the following reasoning applies:

With respect to the subject-matter of claims 1, 12, 13 and 14 the applicant's attention is drawn to the fact that even if novelty could be established over the above-cited prior art it is at present not clear wherein an inventive step may reside.

With respect to the subject-matter of claims 15 and 16 the applicant's attention is drawn to the fact that there seems to be no basis for inventive step within the present application as filed since no evidence can be found that the features which are novel over the prior art contribute to the solution of the posed problem.

It is therefore noted, that the solution proposed in claims 1 and 12-16 of the present application is not considered to be inventive in the sense of Article 33(3) PCT.

The subject-matter of claims 2-11 seems to involve an inventive step in the sense of Article 33(3) PCT as there is no hint in the prior art to solve the technical problem in the way as defined by present claims 2-11.

**Art 33(4)** For the assessment of the present claims 1-16 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.